

REMARKS

Claims 1-36 are pending in the present application. Reconsideration of the application is respectfully requested in view of the following responsive remarks. For the Examiner's convenience and reference, Applicant's remarks are presented in the order in which the corresponding issues were raised in the Office Action.

In the office action of May 31, 2006, the following actions were taken:

- (1) the Examiner pointed out a typo in claim 22;
- (2) claims 2 and 24 were rejected under 35 U.S.C. § 112, second paragraph;
- (3) claims 1-36 were rejected under 35 U.S.C. § 112, second paragraph for neglecting to indicate a point of attachment of the optically active ligand;
- (4) claim 4 was rejected under 35 U.S.C. § 112, second paragraph for lack of antecedent basis; and
- (4) claims 1-36 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Bradley et al (1990, J Org Chem 55:3129-3132) and/or Zhang et al (1997, Chem Rev 99:3313-3361) in view of Cram (U.S. Patent No. 4,001,279).

It is respectfully submitted that the presently pending claims be examined and allowed. Applicants submit that each and every amendment herein, and throughout the prosecution of the present application is fully supported by the specification as originally filed, and that no new matter has been added.

Corrections to claims

The Examiner pointed out that the second line of step (b) of claim 22 contained a typo. The term "bee" has been amended to "been." Withdrawal of this objection is respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 2 and 24 as being indefinite under 35 U.S.C. § 112, second paragraph, for reciting a "means" for performing a specified function without reciting a structure in support of said means. Applicant believes this rejection regarding claim 2 was adequately addressed in the response to the June 13, 2005 Office Action. As the Examiner has not acknowledged or addressed the Applicant's

remarks in the present Office Action, the Applicant believes that the Examiner has not considered them, and they are noted again hereinafter. Applicant reiterates that claim 2 is definite and submits that claim 24 is likewise definite in that they both recite structure with sufficient specificity in the claims and further in view of the specification.

Specifically, claim 2 recites two structures -- B and B', which are set forth in claim 1 as being "independently bulky groups," which sets forth a structural requirement. Likewise, claim 24 recites two structures -- B and B', which are set forth in claim 22 as being "independently bulky groups," which sets forth a structural requirement. Further, the placement and orientation of the bulky groups are also set forth in the respective independent claims. The specification describes "bulky groups" as "branched or unbranched alkyl groups of from 3 to 10 carbons, as well as aromatic groups." See pg. 8, lines 3-5. Based on this description in conjunction with the clear limitations set forth in the claims, claim 2 and claim 24 merely recite further limitation of these structures based on specified function, i.e. steric hindrance of the counter enantiomer. Reciting these structures with further specificity would require naming a limited number of particular substituent groups, which would unduly restrict the scope of these claims. In the absence of relevant prior art, Applicant is entitled to as broad a scope as is supported by the specification. Claims 2 and 24 recite the structures that provide the specified function and that recitation is supported by the specification. Applicant therefore submits that the rejection of claims 2 and 24 should be withdrawn. Reconsideration is respectfully requested.

Claims 2 and 24 were also rejected because the term "substantially" is a relative term, which the Examiner asserts, renders the claims indefinite. In response, the term has been removed from the claims, thereby broadening the scope of the claim language. As this term is no longer in the claim, the Applicant respectfully requests withdraw of the rejections.

Claims 1-36 were rejected as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Particularly, the point of attachment of the optically active ligand to the support is not indicated. Applicant respectfully points out that the point of attachment is indicated inherently in the claims by the definition of the M group for the situations wherein M is tethered to the solid support. It would be apparent to one of ordinary skill in the art

where the possible points of attachment are, when taking into consideration the M group. For example, it is known to those skilled in the art that when M is $-C_2H_4-$, the attachment can be to either carbon. In this instance, the structure looks identical regardless of which carbon is attached. Further, when M is $-C_2H_4OC_2H_4-$, again, it is one of the carbons that is attached, as is known generally in the art. Therefore, the claimed subject matter is properly indicated.

Lastly, claim 4 was rejected as lacking antecedent basis for "pyridyl". Applicant respectfully disagrees, as pyridyl properly refers to an aromatic (see page 8, lines 5-6 of Specification) listed in claim 3. Claim 3 lists aromatic as a possible group for selection of B and B'; and claim 4, depending from claim 3, lists the aromatic compound pyridyl. Thus, there is proper antecedent basis for the inclusion of pyridyl. Reconsideration of each of these rejections under 35 U.S.C. 112 is respectfully requested.

Rejections Under 35 U.S.C. § 103

The Examiner has rejected claims 1-36 as being obvious in view of Bradley et al (1990, J Org Chem 55:3129-3132) and/or Zhang et al (1997, Chem Rev 99:3313-3361) in view of Cram (U.S. Patent No. 4,001,279). The Applicant respectfully submits that these claims are patentable over the cited reference for the reasons set forth below, and that the rejection should be withdrawn.

Before discussing the obviousness rejections herein, it is thought proper to briefly state what is required to sustain such a rejection. The issue under § 103 is whether the PTO has stated a case of *prima facie* obviousness. According to the MPEP § 2142, the Examiner has the burden and must establish a case of *prima facie* obviousness by showing the prior art reference, or references combined, teach or suggest all the claim limitations in the instant application. Further, the Examiner has to establish some motivation or suggestion to combine and/or modify the references, where the motivation must arise from the references themselves, or the knowledge generally available to one of ordinary skill in the art. The Applicant respectfully asserts the Examiner has not satisfied the requirement for establishing a case of *prima facie* obviousness in any of the rejections.

The Bradshaw and Zhang articles present various structures for chiral macrocyclic ligands and various properties thereof as related to enantiomeric

recognition and complexing capacity. These properties were described using data from analyses including calorimetry, NMR spectroscopy, and various types of mass spectrometry. Among the structures described are diketo- and pyridine-containing crown macrocycles.

The present invention provides compositions for selectively binding a preferred target enantiomer over its counter-enantiomer, as well as methods for separating said enantiomers using such compositions. These compositions and methods provide a diketo- and pyridine-containing chiral crown macrocycle that includes two bulky groups that are each attached to chiral carbons of the macrocycle, such as that shown in Figure 1 of the disclosure. These bulky groups contribute to the enantiomeric selectivity of the macrocycle by providing a steric barrier that hinders the counter-enantiomer from complexing thereto. The macrocycle is attached to the solid support and the structure is coated with a hydrophobic organic solvent coating. There are, therefore, at least three distinct elements of the claimed invention: a solid support, an optically active ligand tethered to or coated on the solid support, and a hydrophobic organic solvent coating coated on the solid support.

Bradshaw and Zhang teach a ligand. They do not teach a solid support or a hydrophobic organic solvent coating. Even in combination with Cram, an element remains missing, i.e., the hydrophobic organic solvent coating coated on the solid support. Cram teaches chiral multiheteromacrocycles that include oxygen and binaphthyl unit, from which two pairs of ortho-positioned side chains arise, one pair (designated X) is proximal to the macrocycle, while the other pair (designated Y) is located distal to the macrocycle.

It is inherently impossible for Bradshaw and Zhang to teach the missing element, as they do not teach a solid support, and therefore cannot teach coating onto the missing solid support. As Cram does not teach the coating element, the three references, either alone or in combination, do not teach all of the elements of the presently claimed invention. By virtue of the missing element(s), a *prima facie* case of obviousness has not been met by the combination of Bradshaw, Zhang, and Cram.

Furthermore, the combination of the references is improper due to no expectation of success in the combination. An excellent summary of how the prior art must be considered to make a case of *prima facie* obviousness is contained in *In re Ehrreich et al.*, 220 U.S.P.Q. 504, 509-511 (CCPA 1979). There the court states that

a reference must not be considered in a vacuum, but against the background of the other references of record. It is stated that the question of a § 103 case is what the reference(s) would "collectively suggest" to one of ordinary skill in the art. However, the court specifically cautioned that the Examiner must consider the entirety of the disclosure made by the reference and avoid combining them indiscriminately.

In finding that the "subject matter as a whole" would not have been obvious in *Ehrreich* the court concluded:

"Thus, we are directed to no combination of prior art references which would have rendered the claimed subject matter as a whole obvious to one of ordinary skill in the art at the time the invention was made. The PTO has not shown the existence of all the claimed limitations in the prior art or any suggestion leading to their combination in the manner claimed by applicants." (underlining added)

Moreover, in *In re Dow Chemical Co.*, 5 U.S.P.Q.2d 1529, (Fed. Cir. 1988), the court states that both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure. The Federal Circuit stated in *In re Carroll*, 202 U.S.P.Q. 571, 572 (Fed. Cir. 1979):

One of the more difficult aspects of resolving questions of non-obviousness is the necessity "to guard against slipping into use of hindsight (citing *Graham v. Deere*). Many inventions may seem obvious to everyone after they have been made...(citation of §103)...Thus, in deciding the issue of obviousness, we must look at the prior art presented from a vantage point in time prior to when the invention was made, and through the eyes of a hypothetical person of ordinary skill in the art.

The Applicant submits further that there is no expectation of success in the prior art to support the combination of references cited by the Examiner. The combination of references is dependent on the substitution of the ligands of the Bradshaw and Zhang references with the binaphthyl unit in Cram. However, Cram teaches that the binaphthyl unit is an essential element to the compositions disclosed therein, in that it serves three functions: (1) it provides, via its X side chains, a steric barrier that hinders a particular enantiomer of a guest molecule from complexing with the macrocycle; (2) it acts as a hinge, in that variation in the dihedral angle between the planes of each naphthalene causes the diameter of the space within the macrocycle

to vary accordingly; and (3) it provides, via its Y side chains, a means of tethering the macrocycle to a solid support.

Therefore, the binaphthyl unit taught in Cram is central both to its enantiomeric recognition and to its attachment of the macrocycles to a solid support. Applicant submits that one skilled in the art in possession of the teachings in Bradshaw and/or Zhang as well as Cram would not have an expectation of successfully using the ligands of Bradshaw and Zhang in the manner of Cram.

Additionally, Cram teaches away from combination with Bradshaw and/or Zhang. As discussed above, Cram teaches the binaphthyl unit to be essential to the combination. Cram therefore teaches away from substitution of the binaphthyl unit. Cram also teaches away from the use and methodology of the present invention in that Cram is concerned with chromatography, whereas the present invention deals specifically in non-chromatographic separation. The processes set forth in claims 22 and 36 do not describe or read on traditional chromatography. The present method claims require removal of the source solution from contact with the composition, contacting the composition with a receiving solution, and recovering the target enantiomer. Conversely, chromatography utilizes a mobile phase where the target composition merely moves more slowly down a column than other mobile phase constituents. Thus, chromatography is not a full-bind and full-release system. Further, the composition of claim 1 is particularly adapted for use in this type of a method (non-chromatographic separation). Cram is about chromatography, and thus is (a) fundamentally compositionally different (e.g., Cram does not use a coating) and (b) are not used for non-chromatographic separations (e.g., Cram teaches of a chromatography method). Such fundamental differences do not lend themselves to the present invention subject matter, and inherently teach away. Reconsideration of the claims is respectfully requested on these grounds.

Further, it appears that the Examiner has made a case that it would be obvious to try attaching Bradley and/or Zhang to a solid support as described in Cram. Even if that is true, still, the organic coating is missing from the combination and it is well established that "obvious to try" does not equal obviousness. Great amounts of time and effort have been expended formulating the structures that are claimed in the instant application. Reconsideration on each of these grounds is respectfully requested.

In light of the foregoing, the Applicant submits that the primary references cited by the Examiner to not support a *prima facie* case of obviousness. The combination of references does not teach each and every element of the present claims. Further, there is no expectation of success in combining the references. Additionally, Cram teaches away from combining the references in the manner indicated by the Examiner, and also teaches away from the proposed method as presently claimed. As such, the Applicant respectfully requests withdraw of the rejection.

Applicants assert that claims 1-36 present allowable subject matter and allowance is respectfully requested. If any impediment to the allowance of these claims remains after consideration of the above remarks, and such impediment could be removed during a telephone interview, the Examiner is invited to telephone the undersigned attorney at (801) 566-6633 so that such issues may be resolved as expeditiously as possible.

Please charge any additional fees except for Issue Fee or credit any overpayment to Deposit Account No. 20-0100.

Dated this 30th day of August, 2006.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Gary H. Oakeson", is written over a horizontal line.

Gary H. Oakeson
Attorney for Applicant
Registration No. 44,266

THORPE NORTH & WESTERN, LLP
8180 South 700 East, Suite 200
Sandy, Utah 84070
(801) 566-6633